Necrotizing Entero Colitis
Diversity in Management

A three year study - Aug2007 to July 2010

A Dissertation submitted in partial fulfillment of M.Ch Branch V (Paediatric Surgery) examination of Dr. M. G. R. Medical University, Tamil Nadu, Chennai, to be held in August 2010.

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Certificate

Certified that the dissertation – entitled "Necrotizing Entero Colitis – Diversity in management" is the bonafide work under taken by Dr. G. GANESH PRABHU under our guidance and supervision, in the Department of Paediatric Surgery, Government Rajaji Hospital, Madurai Medical College, Madurai, during the period of his Postgraduate residency in M. Ch. Paediatric Surgery from 2007 to 2010.

Dr. A. Athigaman, M.S., M.Ch.,
Professor and HOD, Department of Paediatric Surgery,
Madurai Medical College, Madurai.

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Introduction

Necrotizing enterocolitis (NEC) is the most common surgical emergency occurring in neonates. Necrotizing enterocolitis represents a significant clinical problem and affects close to 10% of infants who weigh less than 1500 g, with mortality rates of 50% or more depending on severity. Although it is more common in premature infants, it can also be observed in term and near-term babies.

Necrotizing enterocolitis is a severe inflammatory disorder of the intestine occurring usually in premature infants. It is a major cause of death and morbidity in neonates. In contrast to the improvements during the past 30 years in the outcomes of many conditions affecting premature infants, the mortality rate of 30 to 50 percent for babies with intestinal perforation due to necrotizing enterocolitis remains essentially unchanged.

The standard approach to patients with perforated intestine, necrotic intestine, or both is surgical resection of the involved bowel with the creation of intestinal stomas. In a critically ill premature infant, this entails substantial risks. Primary peritoneal drainage, a minimally invasive operation, has evolved as an alternative. It involves a small abdominal incision with placement of a glove drain

into the peritoneal cavity without a formal laparotomy or bowel resection.

There is considerable controversy regarding which procedure is preferable. In our institution for the past 25 years we were doing laparotomy for all these cases and found unacceptably high mortality. So we decided to do primary peritoneal drainage for these sick babies and the results were analyzed in this study.

History

In 1891, Generish published the first case of NEC. In 1939 Thelander reported 16 cases of perforation of the stomach, 30 of the duodenum, and 39 of the small and large intestines. Many of the patients who had intestinal perforations probably had NEC.

The first report of a successfully treated infant with a localized ileal perforation as a result of NEC is attributed to Agerty et al in 1943. In 1953, Schmid and Quaiser first used the term necrotizing enterocolitis. In 1959, Rossier and colleagues described 15 infants, 14 of whom died of "ulcerative-necrotic enterocolitis of the premature."

In 1964, Bredon et al reported the clinical and radiographic findings of 21 patients with NEC. A year later, Mizrahi et al., reported 18 cases of NEC in premature infants. The incidence of NEC in New York Babies Hospital nursery between 1953 and 1963 was 0.9%, but the disease caused 2.3% of all nursery deaths. In 1975, Santulli et al. hypothesized that development of the disease had three essential components:- Injury to the intestinal mucosa, the presence of bacteria, and the availability of a metabolic substrate.

During the 1960s, treatment of NEC was early surgery. By 1970 it was recognized that with early diagnosis, most patients could

be managed without surgery. In 1978, Bell et al. published a severity - based classification scheme that was helpful in selecting therapy and allowing comparison of outcomes.

In 1979, the International Classification of Diseases established a code for death from NEC, thereby allowing more precise epidemiologic and outcome analyses.

Review of Literature

Primary peritoneal drainage was first attempted in 1976 as a possible treatment for intestinal perforation in the smallest preterm infants in the least stable condition. At the time, the condition of this group of patients was believed to be too unstable to tolerate laparotomy, which was the conventional approach. Several anecdotal reports suggested that peritoneal drainage resulted in the unexpected survival of these infants. Subsequently, some retrospective observational case series reported survival rates with drainage approaching or exceeding those with laparotomy, whereas others suggested that laparotomy was the superior treatment.

In a study conducted by Lawrence Moss et al authors reviewed 475 published cases and 190 unpublished cases of patients who underwent either laparotomy and resection or primary peritoneal drainage. They concluded that selection bias and the inability to determine what factors influenced the treatment assignment precluded meaningful comparisons of these approaches.

In previous observational studies, peritoneal drainage was used in smaller babies in unstable condition because of the beliefs that

these babies may not tolerate laparotomy and may have better outcomes after peritoneal drainage. The findings of their study refute those beliefs. Their results in larger babies are limited by small numbers but do not suggest that, because these babies can "tolerate" laparotomy, it is the best treatment.

In some cases, peritoneal drainage has been used as a temporizing procedure, followed by laparotomy in two to three days. Previous observational studies have suggested that mortality with this approach is higher than with either primary peritoneal drainage or laparotomy alone. The condition of patients undergoing peritoneal drainage often improves slowly. Examination of the clinical status for the first several days after peritoneal drainage of patients who ultimately survive, as compared with those who do not, has shown no discernible differences. This suggests that there is no reliable means to determine which patients are destined to do poorly after primary peritoneal drainage and might be candidates for "salvage" laparotomy.

Several investigators have suggested that the choice of operation in patients with perforated necrotizing enterocolitis should be made on the basis of the presenting radiographic findings. They argue that patients with free intra peritoneal air in the absence of

pneumatosis are most likely to have necrotizing enterocolitis of only a short segment of the intestine or isolated intestinal perforation and are best treated with primary peritoneal drainage. In contrast, patients with pneumatosis may have more extensive intestinal involvement and may benefit from laparotomy and bowel resection. Previous observational data from a large, multicenter study, however, suggested that survival among patients without pneumatosis was not greater with peritoneal drainage than with laparotomy.

Frequency

Frequency varies among nurseries, without correlation with season or geographic location. Outbreaks of necrotizing enterocolitis seem to follow an epidemic pattern within nurseries, suggesting an infectious etiology, although a specific causative organism has not been isolated.

Mortality / Morbidity

The mortality rate ranges from 10% to more than 50% in infants who weigh less than 1500 g, depending on the severity of disease, compared with a mortality rate of 0-20% in babies who weigh more than 2500 g. Extremely premature infants (1000 g) are particularly vulnerable, with reported mortality rates of 40-100%. One study

compared mortality rates for term versus preterm infants and reported rates of 4.7% for term infants and 11.9% for premature babies.

Survivors can have significant short-term and long-term morbidities. Patients with mild disease require GI rest to facilitate resolution of the intestinal inflammatory process. These babies are traditionally kept on a diet of nothing by mouth (NPO) for 7-10 days, making parental hyper alimentation necessary. Many of these babies have difficult intravenous (IV) access. Therefore, the need for prolonged parentral nutrition frequently requires placing central venous catheters, which have attendant risks and complications that include thrombo embolic events and nosocomial infections.

A recent multicenter, retrospective study in Switzerland reported a 29% rate of catheter-related sepsis in patients with Bell stage II kept NPO for longer than 5 days. Prolonged hyper alimentation and the absence of enteral nutrition can cause cholestasis, direct hyper bilirubinemia, and other metabolic complications.

Patients who are severely affected may require intestinal resection during the acute phase of their disease. Any patient can develop strictures, as part of the healing process, which require surgical intervention. In rare and severe necrotizing enterocolitis cases, the entire intestine can be involved, precluding surgical

intervention. Depending on the location and extent of the bowel removed, long-term morbidities can include the need for ileostomy and/or colostomy, repeated surgical procedures, prolonged parental nutrition, short gut and mal absorption syndromes, failure to thrive due to sub optimal nutrition, and multiple hospitalizations. Intestinal transplantation for babies with severe short-gut syndrome is becoming more common. Combination liver and small bowel transplantation may be necessary for severely affected infants who have also acquired life-threatening hyper alimentation hepatitis.

Race

Although some studies indicate a higher frequency in black babies than in white babies, other studies show no difference based on race.

Sex

Most studies indicate that male and female babies are equally affected.

Age

Necrotizing enterocolitis is more prevalent in premature infants, with incidence inversely related to birth weight and gestational age. Although specific numbers range from 4% to more than 50%, infants who weigh less than 1000 g at birth have the highest attack rates.

This rate dramatically drops to 3.8 per 1000 live births for infants who weigh 1501-2500 g at birth. Similarly, rates profoundly decrease for infants born after 35-36 weeks' post conceptional. Average age at onset in premature infants seems to be related to post conceptional age, with babies born earlier developing necrotizing enterocolitis at a later chronologic age. The average age of onset has been reported to be 20.2 days for babies born at less than 30 weeks' estimated gestational age (EGA), 13.8 days for babies born at 31-33 weeks' EGA, and 5.4 days for babies born after 34 weeks' gestation.

Infants with patent ductus arteriosus are at higher risk for developing the disease, particularly if pharmacologic closure is attempted. These infants may develop the disease sooner than infants without patent ductus arteriosus.

Term infants develop necrotizing enterocolitis much earlier, with the average age of onset within the first week of life or, sometimes, within the first 1-2 days of life. Observational studies have suggested the patho physiology of the disease in term and near-term infants may be different than that postulated in the premature infant and could include entities such as cow's milk protein–induced enterocolitis and glucose-6-phosphate dehydrogenase deficiency.

The recently reported finding that affected term infants with congenital heart disease, another known risk factor, have decreased risk of major short and long-term adverse outcomes further supports an alternative pathogenetic model.

Etiology

Although the exact etiology remains unknown, research suggests that it is multi factorial; ischemia and/or reperfusion injury, exacerbated by activation of pro inflammatory intracellular cascades, may play a significant role. Cases that cluster in epidemics suggest an infectious etiology. Gram-positive and gram-negative bacteria, fungi, and viruses have all been isolated from affected infants; however, many infants have negative culture findings.

Furthermore, the same organisms isolated in stool cultures from affected babies have also been isolated from healthy babies. Extensive experimental work in animal models suggests that translocation of intestinal flora across an intestinal mucosal barrier rendered vulnerable by the interplay of intestinal ischemia, immunologic immaturity, and immunological dysfunction may play a role in the pathogenesis of the disease, spreading it and triggering systemic involvement. Such a mechanism could account for the

apparent protection breast-fed infants have against fulminant necrotizing enterocolitis.

Pathogenesis

Animal model research studies have shed light on the pathogenesis of this disease. Regardless of the triggering mechanisms, the resultant outcome is significant inflammation of the intestinal tissues, the release of inflammatory mediators (e.g., leukotrienes, tumor necrosis factor [TNF], platelet-activating factor [PAF]) and intra luminal bile acids, and down-regulation of cellular growth factors, all of which lead to variable degrees of intestinal damage. Although the pathogenesis of necrotizing enterocolitis remains uncertain, a large body of evidence suggests a multi factorial etiology, including the presence of abnormal bacterial flora, intestinal ischemia, reperfusion injury with activation of pro inflammatory cellular cascades, and intestinal mucosal immaturity/dysfunction.

- Abnormal intestinal flora
  - In healthy individuals, the intestinal milieu is characterized by a predominance of bifido bacteria. Such colonization is enhanced by the presence of oligo fructose, a component of human milk, in the intestinal lumen. Infants who receive formula feedings without oligo

fructose as a constituent have been noted to have a predominance of clostridial organisms.

- Rat pups colonized with Staphylococcus aureus and Escherichia coli demonstrated increased incidence and severity of necrotizing enterocolitis compared with those whose intestines were populated with various bacterial species. Toll-like receptor signaling of intestinal mucosal trans membrane proteins is accomplished by binding of specific bacterial ligands that mediate the inflammatory response; the character of the intestinal bacterial milieu is thought to play a role in the up-regulation or down-regulation of intestinal inflammation via toll-receptor signaling.
- Many preterm infants receive frequent exposure to broad-spectrum antibacterial agents, further altering the intra-intestinal bacterial environment.
- Experimental and meta-analytical evidence suggests that exogenous administration of the probiotics bifido bacteria and lactobacilli or probiotics (non digestible substances that selectively promote the growth of beneficial probiotic like bacteria normally present in the gut) may moderate the risk and severity of necrotizing enterocolitis in preterm infants.

- Intestinal ischemia

- Epidemiologically, some have noted that infants exposed to intrauterine environments marked by compromised placental blood flow (i.e., maternal hypertension, preeclampsia, cocaine exposure) have an increased incidence of necrotizing enterocolitis. Similarly, infants with post natally diminished systemic blood flow, such as is found in patients with patent ductus arteriosus or congenital heart disease, also have an increased incidence. However, a recent retrospective analysis compared outcomes of necrotizing enterocolitis in patients with congenital heart disease with outcomes of necrotizing enterocolitis in patients without congenital heart disease; the study demonstrated improved outcomes in patients with heart disease. This somewhat counter intuitive finding further emphasizes the multi factorial patho physiology underlying necrotizing enterocolitis.
- Animal models of induced intestinal ischemia have identified its significant role in the development of necrotizing enterocolitis. Pathologically, ischemia induces a local inflammatory response that results in activation of a pro inflammatory cascade with mediators such as PAF, TNF-a, complement, prostaglandins, and leukotrienes such as C4 and IL-18. Alterations in hepato biliary cell junction integrity results in leakage of these pro inflammatory substances and bile acids into the intestinal lumen, increasing intestinal injury. Cellular protective mechanisms such as epidermal growth factor (EGF),

transforming growth factor β1 (TGF-β1), and erythropoietin are down-regulated, further compromising the infant's ability to mount a protective response. Subsequent nor epinephrine release and vasoconstriction results in splanchnic ischemia, followed by reperfusion injury.

- Intestinal necrosis results in breach of the mucosal barrier, allowing for bacterial translocation and migration of bacterial endo toxin into the damaged tissue. The endo toxin then interacts synergistically with PAF and a multitude of other pro inflammatory molecules to amplify the inflammatory response.
  - Activated leukocytes and intestinal epithelial xanthine oxidase may then produce reactive oxygen species, leading to further tissue injury and cell death. Experimental administration of PAF inhibitors in animal models has not been shown to mitigate intestinal mucosal injury. Many other modulators of the inflammatory response are being studied both in vivo in animal models and in vitro in an attempt to mitigate or prevent the morbidity and mortality caused by fulminant necrotizing enterocolitis.
- Intestinal mucosal immaturity
  - In the preterm infant, mucosal cellular immaturity and the absence of mature anti oxidative mechanisms may render the mucosal barrier more susceptible to injury. Intestinal regulatory T-cell

aggregates are a first-line defense to luminal pathogens and may be induced by collections of small lymphoid aggregates, which are absent or deficient in the premature infant.

- Experimental and epidemiologic studies have noted that feeding with human milk has a protective effect; however, donor human milk that has been pasteurized is not as protective. Human milk contains secretory immune globulin A (IgA), which binds to the intestinal luminal cells and prohibits bacterial transmural translocation. Other constituents of human milk, such as interleukin (IL)-10, EGF, TGF-β1, and erythropoietin may also play a major role in mediating the inflammatory response. Oligo fructose encourages replication of bifido bacteria and inhibits colonization with lactose-fermenting organisms.
- Human milk has been found to contain PAF acetyl hydrolase, which metabolizes PAF; preterm human milk has higher PAF acetyl hydrolase activity (as much as 5 times greater in one study) than milk collected from women who delivered at term.

- Innate genetic predisposition

- Twin studies have suggested susceptibility to necrotizing enterocolitis may be affected by a genetic component. Given the frequent subtle and nonspecific nature of presenting symptoms, identification of a biomarker for infants at higher risk of developing

necrotizing enterocolitis could have significant impact on morbidity and mortality rates. Animal models have focused on single-nucleotide polymorphisms (SNPs) that negatively affect innate immune responses to bacterial antigens. One such SNP discovered in the gene that encodes carbamoyl-phosphate synthetase I, the rate-limiting enzyme for the production of Arginine, has been reportedly associated with an increased risk of necrotizing enterocolitis.

o Infants with distinct genotypes of various cytokines have also been associated with higher frequencies of necrotizing enterocolitis. Given the interplay of inherent, infectious, ischemic, inflammatory, iatrogenic, and environmental factors, alterations in expression of pro inflammatory and/or anti-inflammatory mediators may play a role in neonatal susceptibility to the disease.

Patho physiology

Necrotizing enterocolitis affects the GI tract and, in severe cases, can cause profound impairment of multiple organ systems. Initial symptoms may be subtle and can include one or more of the following:-

- Feeding intolerance
- Delayed gastric emptying
- Abdominal distention, abdominal tenderness, or both

- Ileus / decreased bowel sounds
- Abdominal wall erythema (advanced stages)
- Hematochezia

Systemic signs are nonspecific and can include any combination of the following:

- Apnea, Lethargy, Decreased peripheral perfusion, Shock (in advanced stages), Cardiovascular collapse, Bleeding diathesis (consumption coagulopathy),

Nonspecific laboratory abnormalities can include the following:

- Hyponatremia, Metabolic acidosis, Thrombocytopenia, Leukopenia or leukocytosis with left shift, Neutropenia, Prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT), decreasing fibrinogen, rising fibrin split products (in cases of consumption coagulopathy)

History

In patients with necrotizing enterocolitis (NEC), epidemiologic studies demonstrate that demographics, risk factors, patient characteristics, and clinical course differ significantly between term and preterm infants.

- Term baby

  - Compared with a preterm infant, the term baby with necrotizing enterocolitis presents at a younger age, with a reported median age of onset that ranges from 1-3 days of life in the immediate postnatal period, but may appear as late as one month of age.
  - The term neonate who is immediately affected post natally is usually systemically ill with other predisposing conditions, such as birth asphyxia, respiratory distress, congenital heart disease, metabolic abnormalities, or has a history of abnormal fetal growth pattern.
  - Maternal risk factors that reduce fetal gut blood flow, such as placental insufficiency from acute disease (e.g., pregnancy-induced hypertension), chronic disease (e.g., diabetes), or maternal cocaine abuse, can increase the baby's risk for developing necrotizing enterocolitis.
  - Specific signs and symptoms that may be part of the history include bilious vomiting or gastric aspirates, abdominal distention, passage of blood per rectum, abdominal radiographs that reveal dilated loops of bowel, pneumatosis intestinalis, free abdominal air, and other signs of systemic infection, including shock and acidosis.

- Premature baby

- Premature babies are at risk for developing necrotizing enterocolitis for several weeks after birth, with the age of onset inversely related to gestational age at birth.
- Premature infants with patent ductus arteriosus are at higher risk of developing necrotizing enterocolitis earlier in life, particularly if treated with Indomethacin for pharmacologic closure. However, patients with persistent patent ductus arteriosus that ultimately required surgical ligation had a higher necrotizing enterocolitis mortality rate than those whose patent ductus arteriosus were successfully closed without surgery.
- Patients are typically advancing on enteral feedings or may have achieved full-volume feeds when symptoms develop.
- Increased incidence in the post transfusion period has been reported in otherwise healthy premature babies who are feeding enterally and undergo blood transfusion for asymptomatic anemia of prematurity.
- Presenting symptoms may include subtle signs of feeding intolerance that progresses over several hours to a day, subtle systemic signs that may be reported enigmatically by the nursing staff as "acting different," and, in advanced disease, a fulminant systemic collapse and consumption coagulopathy.

- Symptoms of feeding intolerance can include abdominal distention/tenderness, delayed gastric emptying as evidenced by increasing gastric residuals, and, occasionally, vomiting.
- Systemic symptoms can insidiously progress to include nonspecific signs and symptoms, such as increased apnea and brady cardia, lethargy, and temperature instability representing the primary manifestation(s).
- Patients with fulminant necrotizing enterocolitis present with profound apnea, rapid cardiovascular and hemodynamic collapse, and shock.
- The baby's feeding history can help increase the index of suspicion for early necrotizing enterocolitis. Babies who are breastfed have a lower incidence of necrotizing enterocolitis NEC than formula-fed babies.
- Rapid advancement of formula feeding has been associated with an increased risk of necrotizing enterocolitis. However, multiple subsequent studies have failed to substantiate this finding.

Physical

- The pertinent physical findings in patients who develop necrotizing enterocolitis can be primarily GI, primarily systemic, indolent, fulminant, or any combination of these. A high index of

clinical suspicion is essential to minimize potentially significant morbidity or mortality.

- GI signs can include any or all of the following:
  - Increased abdominal girth
  - Visible intestinal loops
  - Obvious abdominal distention and decreased bowel sounds
  - Change in stool pattern
  - Hematochezia
  - A palpable abdominal mass
  - Erythema of the abdominal wall
- Systemic signs can include any of the following:
  - Respiratory failure
  - Decreased peripheral perfusion
  - Circulatory collapse
  - With insidious onset, the clinical signs may be mild, whereas patients with fulminant disease can present with severe clinical abnormalities.

Laboratory Studies

- Initial presentation of necrotizing enterocolitis (NEC) usually includes subtle signs of feeding intolerance, such as gastric residuals,

abdominal distention, and/or grossly bloody stools. Abdominal imaging studies are crucial at this stage. In fact, radiographic studies should be obtained if any concern about necrotizing enterocolitis is present. Laboratory studies are pursued, especially if the abdominal study findings are worrisome or the baby is manifesting any systemic signs.

- CBC count, with manual differential to evaluate the WBC, hematocrit, and platelet count, is usually repeated at least every 6 hours if the patient's clinical status continues to deteriorate.

o WBC count: Marked elevation may be worrisome, but Leukopenia is even more concerning. Although elevated mature and/or immature Neutrophil counts may not be good indicators of neonatal sepsis after the first 3 days of life, moderate-to-profound Neutropenia (absolute Neutrophil count [ANC] <1500/μL) strongly suggests established sepsis.

o RBC count:- Premature infants are prone to anemia due to iatrogenic blood draws, as well as anemia of prematurity; however, blood loss from Hematochezia and/or a developing consumptive coagulopathy can manifest as an acute decrease in hematocrit.

o Platelet count: Platelets are an acute phase reactant, and thrombocytosis can represent physiologic stress to an infant, but acute necrotizing enterocolitis is more commonly associated with

thrombocytopenia (<100,000/μL). Thrombocytopenia may become more profound in severe cases that become complicated with consumption coagulopathy. Consumption coagulopathy is characterized by prolonged PT, prolonged aPTT, and decreasing fibrinogen and increasing fibrin degradation products concentrations.

- Blood culture: Obtaining a blood culture is recommended before beginning antibiotics in any patient presenting with any signs or symptoms of sepsis or necrotizing enterocolitis. Although blood cultures do not grow any organisms in most cases of necrotizing enterocolitis, sepsis is one of the major conditions that mimics necrotizing enterocolitis and should be considered in the differential diagnosis. Therefore, identification of a specific organism can aid and guide further therapy.

- Serum electrolytes can show some characteristic abnormalities. Obtain basic electrolytes ($Na^{+,}$ K^{+}, and Cl^{-}) during the initial evaluation, followed serially at least every 6 hours depending on the acuity of the patient's condition.

- Serum sodium:- Hyponatremia is a worrisome sign that is consistent with capillary leak and "third spacing" of fluid within the bowel and peritoneal space. Depending on the baby's age and feeding regimen, baseline sodium levels may be low-normal or

subnormal, but an acute decrease (<130 mEq/dL) is alarming and heightened vigilance is warranted.

- Metabolic acidosis: Low serum bicarbonate (<20) in a baby with a previously normal acid-base status is also concerning. It is seen in conjunction with poor tissue perfusion, sepsis, and bowel necrosis.

- Arterial blood gasses

- Depending on presentation acuity, hypoventilation and frank apnea are seen in necrotizing enterocolitis. ABG can aid in the determination of the infant's need for respiratory support. The ABG can also provide information of the acid-base status.

- Acute acidosis is worrisome. Lactic acidosis results from decreased cardiac output (as in cardiovascular collapse and shock), leading to poor perfusion of peripheral tissues. Tissue necrosis may also add to the observed metabolic acidosis.

- An arterial blood sample is a convenient way to simultaneously obtain a blood culture, CBC count, serum electrolytes, and ABG for the initial evaluation (note that arterial blood has a lower yield for demonstrating bacteremia than venous blood). Depending on presentation acuity, inserting a peripheral arterial line while peripheral perfusion and intravascular volume is still within the reference range may be prudent. This peripheral arterial line facilitates serial blood

sampling and invasive blood pressure monitoring that is essential if the baby's condition deteriorates.

- Although all of these initial laboratory studies taken together may aid in the diagnosis of necrotizing enterocolitis, they do not substitute for an appropriate appreciation of clinical presentation and appearance of the infant. The laboratory values can give insight into the severity of the disease and can aid in the provision of appropriate therapy.

Imaging Studies

- The mainstay of diagnostic imaging is abdominal radiography. An antero posterior (AP) abdominal radiograph and a left lateral decubitus radiograph (left-side down) are essential for initially evaluating any baby with abdominal signs. Perform abdominal radiography serially at 6-hour or greater intervals, depending on presentation acuity and clinical course.
  - Characteristic findings on an AP abdominal radiograph include an abnormal gas pattern, dilated loops, and thickened bowel walls (suggesting edema/inflammation). Serial radiographs help assess disease progression. A fixed and dilated loop that persists over several examinations is especially worrisome.

- Radiographs can sometimes reveal scarce or absent intestinal gas, which is more worrisome than diffuse distention that changes over time.
- **Pneumatosis intestinalis** is a radiologic sign pathognomic of necrotizing enterocolitis. It appears as a characteristic train-track lucency configuration within the bowel wall. Intramural air bubbles represent gas produced by bacteria within the wall of the bowel. Analysis of gas aspirated from these air bubbles reveals that it consists primarily of hydrogen, suggesting that these are caused by bacterial fermentation. Carbohydrate (often lactose) fermentation by intestinal flora yields hydrogen and carbon dioxide and a series of short-chain organic acids, which can promote inflammation.
- Abdominal free air is ominous and usually requires emergency surgical intervention. The presence of abdominal free air can be difficult to discern on a flat radiograph, which is why decubitus radiographs are recommended at every evaluation. A subtle oblong lucency over the liver and abdominal contents is characteristic of intra peritoneal air on a flat plate. It represents the air bubble that has risen to the most anterior aspect of the abdomen in a baby lying in a supine position. The free air can be difficult to differentiate from intra luminal air.

- For this reason, left-side down (left lateral) decubitus radiography is essential and allows the detection of intra peritoneal air, which rises above the liver shadow (right-side up) and can be visualized easier than on other views. Obtain this view with every AP examination until progressive disease is no longer a concern.
- Portal gas is thought to be ominous when detected. Portal gas appears as linear branching areas of decreased density over the liver shadow and represents air present in the portal venous system. Its presence is considered a poor prognostic sign. Portal gas is much more dramatically observed on Ultrasonography.
- Ascitis is a late finding that usually develops when peritonitis is present or after bowel perforation. Ascitis is observed on an AP radiograph as centralized bowel loops that appear to be floating on a background of density. It is better appreciated on Ultrasonography.

• Abdominal Ultrasonography can be helpful when suspected necrotizing enterocolitis in neonates is evaluated.

- Ultrasonography can be used to identify areas of loculation and/or abscess consistent with a walled-off perforation when patients with indolent necrotizing enterocolitis have scarce gas or a fixed area of radiographic density.

- Ultrasonography is excellent identifying and quantifying ascitis. Serial examinations can be used to monitor the progression of ascitis as a marker for the disease course.
- Portal air can be easily observed as bubbles present in the venous system.

- Doppler study of the splanchnic arteries early in the course of necrotizing enterocolitis can help distinguish developing necrotizing enterocolitis from benign feeding intolerance in a mildly symptomatic baby.
- A clinical study from Europe and a small series in the United States demonstrated markedly increased peak flow velocity (>1) of arterial blood flow in the celiac and superior mesenteric arteries in early necrotizing enterocolitis. Such a finding at the presentation of symptoms can further aid in diagnosis and therapy, potentially sparing those individuals at low risk for necrotizing enterocolitis from unnecessary interventions.

Other Tests

- Reports from outside of the United States suggest that more contemporary imaging techniques, such as contrast radiography, portal vein Ultrasonography, MRI, and radionuclide scanning, may

play a role in diagnosis. These techniques are not currently in common use.

- GI tono metry is an infrequently used technique that may be helpful in distinguishing benign feeding intolerance from early necrotizing enterocolitis.

Procedures

Nonsurgical procedures for necrotizing enterocolitis are as follows:

- Upper GI (with or without) small bowel follow-through is only performed acutely when diagnosis other than necrotizing enterocolitis are being considered (e.g., bowel obstruction) because of bilious vomiting, abdominal distention, or other symptoms. This procedure is commonly performed in infants with resolved necrotizing enterocolitis who develop a picture of GI obstruction, usually due to a stricture or fibrous band. Perform this before contrast enema because the presence of contrast in the colon can obscure pertinent findings.
- Placement of a peripheral arterial line may be helpful at the beginning of the patient's treatment to facilitate serial arterial blood sampling and invasive monitoring.
- Placement of a central venous catheter for administration of pressors, fluids, antibiotics, and blood products is prudent as severely

affected patients often have complications that include sepsis, shock, and disseminated intravascular coagulation (DIC).

- If the baby is rapidly deteriorating, with apnea and/or signs of impending circulatory and respiratory collapse, airway control and initiation of mechanical ventilation is indicated.
- Abdominal decompression in infants with necrotizing enterocolitis is as follows:
  - Decompression is essential at the first sign of abdominal pathology.
  - Use a large-bore catheter with multiple side holes and a second lumen to prevent vacuum attachment to the stomach mucosa (e.g., Replogle tube).
  - Set the catheter for low continuous or intermittent suction and monitor output. The tube should be irrigated with several milliliters of normal saline to maintain patency.
  - If copious amounts of gastric/intestinal secretions are removed, consider intravenous (IV) replacement with a physiologically similar solution. Maintaining electrolyte balance and intravascular volume is essential.
- Ascitis can develop during fulminant necrotizing enterocolitis and can compromise respiratory function. Paracentesis may be considered.

- Place an intra-abdominal drain as an alternative to laparotomy if the baby is not a surgical candidate (e.g., extreme prematurity or cardiovascular collapse and shock).

Treatment

Medical Care

Diagnosis of necrotizing enterocolitis (NEC) is based on clinical suspicion supported by findings on radiologic and laboratory studies. Treatment of necrotizing enterocolitis depends on the degree of bowel involvement and severity of its presentation. Objective staging criteria developed by Bell have been widely adopted or modified to help tailor therapy according to disease severity.

- Bell stage I - Suspected disease
  - Stage IA
- Mild nonspecific systemic signs such as apnea, brady cardia, and temperature instability are present.
  - Mild intestinal signs such as increased gastric residuals and mild abdominal distention are present.
  - Radiographic findings can be normal or can show some mild nonspecific distention.
  - Treatment is kept on a diet of nothing-by-mouth (NPO) with antibiotics for 3 days.

- Intravenous (IV) fluids, including total parentral nutrition (TPN)

  - Stage IB

    - Diagnosis is the same as IA, with the addition of grossly bloody stool.

    - Treatment is NPO with antibiotics for 3 days and IV fluids.

- Bell stage II - Definite disease

  - Stage IIA

    - Patient is mildly ill.

    - Diagnostic signs include the mild systemic signs present in stage IA.

    - Intestinal signs include all of the signs present in stage I, with the addition of absent bowel sounds and abdominal tenderness.

    - Radiographic findings show Ileus and/or pneumatosis intestinalis. This diagnosis is sometimes referred to as "medical" necrotizing enterocolitis as surgical intervention is not needed to successfully treat the patient.

    - Treatment includes support for respiratory and cardiovascular failure, including fluid resuscitation, NPO, and antibiotics for 14 days. Surgical consultation should be considered. After stabilization, TPN should be provided during the period that the infant is NPO.

  - Stage IIB

    - Patient is moderately ill.

- Diagnosis requires all of stage I signs plus the systemic signs of moderate illness, such as mild metabolic acidosis and mild thrombocytopenia.
- Abdominal examination reveals definite tenderness, perhaps some erythema or other discoloration, and/or right lower quadrant mass.
- Radiographs show portal venous gas with or without ascitis.
- Treatment includes support for respiratory and cardiovascular failure, including fluid resuscitation, NPO, and antibiotics for 14 days. Surgical consultation should be considered. After stabilization, TPN should be provided during the period that the infant is NPO.

• Bell stage III - Represents advanced necrotizing enterocolitis with severe illness that has a high likelihood of progressing to surgical intervention.

o Stage IIIA

- Patient has severe necrotizing enterocolitis with an intact bowel.
- Diagnosis requires all of the above conditions, with the addition of hypotension, brady cardia, respiratory failure, severe metabolic acidosis, coagulopathy, and/or Neutropenia.
- Abdominal examination shows marked distention with signs of generalized peritonitis.
- Radiographic examination reveals definitive evidence of ascitis.

- Treatment involves NPO for 14 days, fluid resuscitation, inotropic support, and ventilator support. Surgical consultation should be obtained. TPN should be provided during the period of NPO.

o Stage IIIB

- This stage is reserved for the severely ill infant with perforated bowel observed on radiograph in addition to the findings and treatment recommendations for IIIA.
- Surgical intervention as outlined below.

Surgical Care

- Free air visible on abdominal radiograph is an indication for surgery. Surgical treatment includes resecting the affected portion of the bowel, which may be extensive. Initially, an ileostomy with a mucous fistula is typically performed, with re anastomosis performed later. Strictures may occur, with or without a history of surgical intervention, which may require surgical treatment.
- Patients who are extremely small and ill may not have the stability to tolerate laparotomy. If free air develops in such a patient, one may consider inserting a peritoneal drain under local anesthesia in the nursery.
- The surgical community remains divergent on the risks and benefits of open laparotomy versus peritoneal drain placement. Two

retrospective reviews of the use of peritoneal drains as initial therapy for perforated bowel concluded that, although most patients ultimately require open laparotomy, initial peritoneal drainage may allow systemic stabilization and recovery in the smallest, sickest infants until they become better surgical candidates. More recent prospective randomized trials have failed to show a difference in outcomes between the 2 approaches, although local custom may continue to impact the decision for surgical intervention in patients who are surgical candidates.

- Any patient requiring surgical intervention and many of those patients not progressing to surgery require protracted courses of parental nutrition and IV antibiotics.
  - Secure central venous access is optimal for ensuring uninterrupted delivery of antibiotics and nutrition as well as maximizing nourishment with central venous formulations.
  - Some units successfully use per cutaneously inserted central venous catheters (PCVCs), whereas other units prefer surgically placed central lines such as Broviac catheters. Both types carry an increased risk of infection, particularly if they are used to administer lipids.

Diet

- When necrotizing enterocolitis is suspected, enteral feedings are withheld and parental nutrition is initiated. Centrally delivered formulations with appropriate nutritional components are infused for optimal IV nutrition. Enteral feedings are traditionally restarted 10-14 days after findings on abdominal radiographs normalize in the case of nonsurgical necrotizing enterocolitis. However, balancing the risks and benefits of NPO versus enteral feeds may alter this timeline. Reinitiating enteral feeds in postsurgical babies may take longer and may also depend on issues such as the extent of surgical resection, return of bowel motility, timing of re anastomosis.
- Because of the high incidence of postsurgical strictures, some clinicians prefer to evaluate intestinal patency via contrast studies prior to initiating enteral feeds. When feeds are restarted, if human milk is not available, formulas containing casein hydrolysates, medium-chain triglycerides, and safflower/sunflower oils may be better tolerated and absorbed than standard infant formulas.

Medication

Pharmacologic therapy for necrotizing enterocolitis (NEC) includes agents to treat the developing disease and those to provide

supportive and symptomatic relief. Probiotics are emerging as a possible preventive therapy.

Antibiotic

Although no single infectious etiology is known to cause necrotizing enterocolitis, clinical consensus finds that antibiotic treatment is appropriate. Broad-spectrum parental therapy is initiated at the onset of symptoms after obtaining blood, spinal fluid, and urine for culture. Antibiotic coverage for staphylococcus should be considered in neonatal ICUs (NICUs) that have a high colonization rate. Antifungal therapy should be considered for premature infants with a history of recent or prolonged antibacterial therapy or for babies who continue to deteriorate clinically or hematologically despite adequate antibacterial coverage.

Various antibiotic regimens can be used; one frequently used regimen includes Ampicillin, Amino Glycoside (e.g., Gentamicin) or third-generation cephalosporin (Cefotaxime), and Clindamycin or Metronidazole. Vancomycin should be included if staphylococcus coverage is deemed appropriate. This combination provides broad gram-positive coverage (including staphylococcal species), excellent gram-negative coverage (with the exception of pseudomonas), and anaerobic coverage.

OTHER SUPPORTIVE MEASURES

Vasopressors

Babies with serious illness may progress to shock and require pharmacologic blood pressure support.

Volume expanders

Patients with severe illness may experience fluid shifts to the extracellular space, resulting in intravascular depletion requiring expansion.

Fresh frozen plasma

Used as a volume expander, especially helpful for patients with concomitant coagulopathy.

Gluco cortico steroids

These agents correct the inappropriate adrenal response that is often present in very ill neonates. Once hydrocortisone therapy is initiated, hypotension typically resolves.

Probiotics

Oral administration of nonpathogenic bacterial species may result in beneficial alteration of intestinal bacterial flora, reducing risk and severity of disease.

Lactobacillus acidophilus/Bifidobacterium infantis

Lactic acid–producing organisms thought to acidify the intestinal contents and to prevent selective bacterial growth. Probiotic live

cultures are intended to restore or maintain healthy microbial flora. Data are currently emerging regarding use in NEC. Various products are available and doses may vary between products. Infloran has specifically been studied in NEC among VLBW infants. It has completed phase II clinical trials.

TPN

- In patients with necrotizing enterocolitis (NEC), prolonged parental nutrition is essential to optimize the baby's nutrition while the GI tract is allowed enough time for recovery and return to normal functioning. Central venous access is essential to facilitate parental delivery of adequate calories and nutrients to the recovering premature baby to minimize catabolism and promote growth.
- Prolonged central venous access may be associated with an increased incidence of nosocomial infection, predominately with skin flora such as coagulase-negative Staphylococcus species as well as Methicillin-resistant S aureus (MRSA). A high degree of clinical suspicion must be maintained to detect the subtle signs of such infection as early as possible.
    - Parentral administration of lipid formulations via central venous catheters is also associated with an increased incidence of catheter-related sepsis.

- Lipids coat the catheter's interior, allowing ingress of skin flora through the catheter lumen. A high degree of clinical suspicion is required for early detection of such an infection.
- If line infection is suspected, obtain a blood culture through the central line and from a peripheral vein or artery. Antibiotics effective against skin flora (e.g., Vancomycin) should be administered. Persistently positive cultures require removing the central line. Remove the central line once sepsis and bacteremia are confirmed because eradication is almost impossible when the central line is kept in place.

- Prolonged parental nutrition may be associated with cholestasis and direct hyper bilirubinemia. This condition resolves gradually following initiation of enteral feeds.
- Prolonged broad-spectrum antibacterial therapy increases the premature infant's risk for fungal sepsis

Complications

Approximately 75% of all patients survive, with those requiring surgical intervention during the acute phase of the disease demonstrating much lower survival rates. Of those patients who survive, 50% develop a long-term complication. The 2 most common complications are intestinal stricture and short-gut syndrome.

- Intestinal strictures

  - This complication can develop in infants with or without a preceding perforation.
  - Incidence is 25-33%.
  - Although the most likely location for acute disease is the terminal ileum, strictures most commonly involve the left side of the colon.
  - Symptoms of feeding intolerance and bowel obstruction typically occur 2-3 weeks after recovery from the initial event.
  - The presence and location of the obstruction is diagnosed using contrast enema; surgical resection of the affected area is required. Many surgeons routinely perform contrast enemas in their patients before bowel re anastomosis so that all necessary surgical intervention can be performed at one time.

- Short-gut syndrome

  - This is a mal absorption syndrome resulting from removal of excessive or critical portions of small bowel necessary for absorption of essential nutrients from the intestinal lumen.
  - Symptoms are most profound in babies who either have lost most of their small bowel or have lost a smaller portion that includes the ileo cecal valve.

- Loss of small bowel can result in mal absorption of nutrients as well as fluids and electrolytes.
- The neonatal gut grows and adapts over time, but long-term studies suggest that this growth may take as long as 2 years to occur. During that time, maintenance of an anabolic and complete nutritional state is essential for the growth and development of the baby. This is achieved by parental provision of adequate vitamins, minerals, and calories; appropriate management of gastric acid hyper secretion; and monitoring for bacterial overgrowth. The addition of appropriate enteral feedings during this time is important for gut nourishment and remodeling.
- Babies who can never successfully feed enterally, and/or who develop life-threatening hyper alimentation liver disease, may be candidates for organ transplantation. Centers specializing in neonatal and infant small bowel and liver transplantation may consider referrals on a case-by-case basis.

Keeping all the above facts in mind we conducted this study in our institution.

Aims and objectives

To improve the results of NEC with established perforation as evidenced by pneumo peritoneum. The treatment protocol was that of conservative management. Primary peritoneal drainage – Glove Flank drain was done bilaterally in lieu of Surgery as the primary modality and the results were analyzed.

Glove drain was chosen in place of tube, sump, rubber or PVC drain considering the nature of the soft, inflamed, brittle, distended bowel which perforates even at the slightest provocation. We felt that a soft rubber drain would effectively drain the peritoneal cavity and keep the drainage route patent, while at the same time it would not harm the bowel.

Patients and methods

INCLUSION CRITERIA

All cases of perforated neonatal NEC proven by radiographic study; i.e. gas under diaphragm, irrespective of the weight.

EXCLUSION CRITERIA

Nil.

STUDY PERIOD

October 2007 to February 2010.

PLACE OF STUDY CONDUCTED

Dept. of Paediatric Surgery, Govt. Rajaji hospital, Madurai.

METHODOLOGY

All babies with perforated NEC after confirmation with radiograph received a 1/4-in. (0.6-cm), full-thickness incision in the both lower quadrants of the abdomen. Stool and pus were expressed manually from the peritoneal cavity. Bilaterally long, glove drains were placed by means of the incision in the lower quadrant and routed to all quadrants of the abdomen. After the procedure, all babies were kept in NICU, with oxygen support and warmer. Intravenous fluids were given according to serum electrolytes. According to the

protocol, all babies were given the same intravenous antibiotics-[Pipercillin, Amikacin and Metrogyl].

After 48 hours, baby‘s general condition was assessed. If there was no improvement or further deterioration, the protocol allowed for laparotomy particularly in patients with persistent metabolic acidosis, hemodynamic instability, and respiratory failure. If the peritoneal cavity was believed to be inadequately drained, on the basis of the re-accumulation of air or fluid in the abdomen, the original drain was manipulated. TPN was given for all babies until oral feeds were started.

Oral feeds were started once the baby started passing stools and abdomen settles. Drains were removed subsequently once there was no leak from drain site. Babies were discharged seven days after starting oral feeds and after confirming passage of normal stools.

OUTCOMES MEASURED

1. Mortality
2. Morbidity and Complications
3. Number of hospital days.

Observations

During the study period from October 2007 to February 2010, a total of ten cases of perforated neonatal NEC were included in the study and we observed the following results. In our study, we observed that all babies were initially admitted in Paediatric NICU and then referred to surgical side once they develop pneumo peritoneum.

Bilateral flank drains were inserted after stabilizing the cases with intravenous fluids. In all ten cases, air was the predominant one that came out immediately after inserting drains along with some biliopurulent material.

On analyzing the cases 48 hours after the procedure, in eight out of ten cases, the general condition improved dramatically.

In our study, 8 out of 10 babies were treated successfully by primary peritoneal drainage. Two cases expired [table 1]. One case was very sick at the time of transfer from paediatric NICU itself and was on ionotrope support, preterm and very low birth weight [1100 gm]. Other case died of sepsis on second day.

All the 8 babies who were treated successfully by peritoneal drainage started passing stools per rectally between fifth to seventh day post procedure.

The average time taken for starting oral feeds in these 8 babies was 7 to 9 days. Drains were removed between 10 to 12 days depending on the day of starting oral feeds.

Four cases needed manipulation or re-adjustment of drains. Two cases had localized collections intra-peritoneally and needed ultrasound to locate the site of collections and subsequently drained by re adjusting the drains.

The mean number of days of hospital stay was 18 to 20 days. On follow up, seven cases had no complications and had good weight gain and normal feeding patterns. One baby was readmitted with features of adhesive intestinal obstruction and was treated successfully with conservative management.

On analyzing the peri natal history, two mothers had maternal risk factor of eclampsia. There was no history of maternal intake of cocaine or xanthine derivatives.

Out of 10 cases, 8 were preterm and low birth weight babies. There was history of birth asphyxia in 7 cases [table 4].

The feeding pattern is shown in table 5. Only 3 babies received exclusive mother's feed, while remaining 7 received both mother's feed and formula feeds.

There was history of NICU admissions in outside hospitals where they were born in 8 babies, before they were referred here [table 7].

The results of blood culture and CRP are shown in table 9. Blood culture was positive only in 20 % of cases where as CRP was positive in 90 % of cases.

Tables

Table 1. Mortality Rate [Peritoneal drainage group]

Total no. of cases	10	Rate
Treated successfully	8	80%
Expired	2	20%

Table 2. Mortality Rate [Laparotomy Group]

Total no. of cases	22	Rate
Treated successfully	6	27.3%
Expired	16	72.7%

Table 3. Mode Of Delivery

Mode of delivery	No. of cases
Normal vaginal delivery	3
LSCS	3
Forceps	6

Table 4. Birth Asphyxia

Birth Asphyxia	**No. of cases**
Yes	**7**
No	**3**

Table 5. Feedings

Feedings	**No. of cases**
Exclusive mother's feed	3
Formula feed	2
Both	5

Table 6. Maturity & Weight

Characteristics	No. of cases
Maturity-	
Term	2
Preterm	8
Birth weight	
>2 kg	4
<2 kg	6

Table 7. NICU Admissions

Paediatric NICU Admissions	No. of cases
Yes	**8**
No	**2**

Table 8. APGAR score

APGAR score	No. of cases
One minute Apgar score	
<3	2
3-6	4
>6	4
Five minutes Apgar score	
<5	2
6-7	3
>7	5

Table 9. Blood culture & CRP

	Positive	Negative
Blood culture	2	8
CRP	9	1

Discussion

In our institution, for the past twenty years laparotomy and either stoma creation or bowel resection and anastomosis was the primary treatment modality for all the cases of perforated neonatal NEC. Since these babies were too sick and under weight to withstand a major surgical procedure, the mortality rate was unacceptably high [>72%].

When we did primary peritoneal drainage for couple of sick cases who were declared unfit for anesthesia for laparotomy, surprisingly we found good results. So we decided to switch over to primary peritoneal drainage for all cases of perforated neonatal NEC irrespective of their weight and conducted this prospective study and analyzed the results.

During the study period, totally ten cases were included. All the cases, whether born in our hospital or out side hospitals, were admitted initially in Paediatric NICU and then referred to surgical NICU once they developed perforation. After stabilizing them, Peritoneal drainage was done for all these cases, in the procedure room under local anesthesia after obtaining informed written consent from the parents.

After the procedure all the babies were kept in neonatal warmer with oxygen support. All cases received same antibiotics- injections Pipercillin, Tazobactam combination, Amikacin and Metrogyl. Intra venous fluids given and electrolytes checked periodically.

On analyzing the old records over the past five years, we found >72% mortality rate for the cases who underwent laparotomy for perforated NEC. In our study, out of ten cases 8 survived and only two expired with mortality rate of 20 %. This clearly shows that Peritoneal drainage is far superior than laparotomy and extensive surgical procedures in these sick and moribund babies grappling for life.

In perforated NEC, during laparotomy invariably we can find extensive adhesions, papery thin bowel with large areas of bowel necrosis and perforations. These adhesions when released invariably leads to more damage and extensive bowel resection. There is high chance of fecal fistula in such cases, which is more difficult to manage and ultimately one surgery may lead to many surgeries.

All cases were vigorously monitored and status re-assessed at 48 hours. According to the protocol, laparotomy was allowed if the condition deteriorates. In our study all the 8 cases who survived showed signs of improvement at 48 hours and there was no need for laparotomy even in a single case. This was due to the decompression

of air and toxic materials from peritoneal cavity and subsequent improvement in hemo-dynamic status.

In our study two cases expired. One baby was too sick at the time of admission itself and was preterm and weighing only 1100 Gm. That particular baby was already on vasopressors and in de-arranged metabolic status and respiratory distress. This case expired within an hour after admission. The other case expired on second day due to sepsis. Both the cases were too sick to such an extent that they would have died even without peritoneal drainage.

Blood culture, complete hemogram, serum electrolytes and ABG were done for all cases. Blood culture was positive in 2 cases and CRP in 9 cases. CRP is a sensitive marker for sepsis, but it is not a specific test for NEC because it will be raised in many other conditions.

In our study most of the babies had mild to moderate metabolic acidosis. Depending on presentation acuity, hypoventilation and frank apnea are seen in necrotizing enterocolitis. ABG can aid in the determination of the infant's need for respiratory support. The ABG can also provide information of the acid-base status.

Acute acidosis is worrisome. Lactic acidosis results from decreased cardiac output (as in cardiovascular collapse and shock),

leading to poor perfusion of peripheral tissues. Tissue necrosis may also add to the observed metabolic acidosis.

Most of the babies started passing stools after 5 days and orals feeds were allowed after that. Till that time TPN was given. Drains were removed if there was no further leak after starting oral feeds. Four cases needed re adjustment of drains. Two cases had pockets of localized collections. Ultrasonogram was done for these babies and collections were drained by manipulating the drains. All cases were followed up every week for first month and subsequently once in a month. Out of the 8 who survived one baby was re-admitted with features of adhesive intestinal obstruction and was managed conservatively.

On analyzing the risk factors for NEC in our study group, we got history of birth asphyxia in 7 cases. Pathologically, ischemia induces a local inflammatory response that results in activation of a pro inflammatory cascade with mediators such as PAF, TNF-a, complement, prostaglandins, and leukotrienes such as C4 and IL-18. Alterations in hepato biliary cell junction integrity results in leakage of these pro-inflammatory substances and bile acids into the intestinal lumen, increasing intestinal injury. Subsequent nor epinephrine release and vasoconstriction results in splanchnic ischemia, followed

by reperfusion injury. When analyzing maternal risk factors we found three mothers having history of maternal hypertension and preeclampsia. The cause of NEC in this group is due to compromised placental blood flow. There was no history of cocaine intake or any medicines that cause vaso-constriction like aminophylines.

Preterm or prematurity is one of the major risk factor for NEC. In our study 8 cases were preterm. In the preterm infant, mucosal cellular immaturity and the absence of mature anti oxidative mechanisms may render the mucosal barrier more susceptible to injury. Intestinal regulatory T-cell aggregates are a first-line defense to luminal pathogens and may be induced by collections of small lymphoid aggregates, which are absent or deficient in the premature infant. In our study, 7 out of ten babies received formula feeds and only 3 received exclusive breast milk. Human milk contains secretory immunoglobulin A (IgA), which binds to the intestinal luminal cells and prohibits bacterial transmural translocation. Other constituents of human milk, such as interleukin (IL)-10, EGF, TGF-β1, and erythropoietin may also play a major role in mediating the inflammatory response. Oligo fructose encourages replication of bifido bacteria and inhibits colonization with lactose-fermenting organisms.

Summary

Due to unacceptably high mortality rate of more than 72% in cases who underwent laparotomy for perforated NEC in our centre over the last five years, we switched over to primary peritoneal drainage and analyzed the results in this study. During the study period, primary peritoneal drainage was done for all cases of perforated NEC [n=10]. Out of ten cases eight survived and two cases expired with mortality rate of 20%. The two cases who expired were grossly under weight and pre term and survival even without this complication would have been a remote possibility.

Only one case was re-admitted with features of adhesive intestinal obstruction and was managed conservatively. On analyzing the perinatal risk factors, we found birth asphyxia, prematurity and weight as very high risk factors for NEC. There was history of birth asphyxia in 7 cases (70%). Eight cases were preterm (80%) and six out of ten babies weigh less than 2 kg.

Seven cases received formula feeds and ultimately developed NEC. Blood culture was positive in only 20% of the cases where as CRP was positive in 90 % of cases. The mean hospital stay in our study was 18 to 20 days from the day of procedure.

Conclusion

- The mortality rate of cases of perforated NEC treated with primary peritoneal drainage is 20 % when compared to more than 72% in those who underwent laparotomy.
- All cases of perforated NEC are now treated exclusively by primary peritoneal drainage in our instituition since the results are far superior and better than the laparotomy results.
- Since this is a small study with limited follow-up, this has to be followed up and corroborated by others.
- Time and future will stand testimony to this treatment.

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